REMARKS

The Amendment, filed in response to the Office Action dated December 4, 2009, is believed to fully address all and every issues raised in the Office Action. Favorable reconsideration and allowance of the application are respectfully requested.

Applicants thank the Examiner for withdrawing previous rejections in view of Applicant's arguments and/or amendments.

Summary of Amendment and Claims Disposition

Claims 1-6, 8, 9, 11-13, 15, and 16 are all the claims pending in the application. Claim 15 is withdrawn from consideration as being directed to non-elected subject matter. In the Office Action dated December 4, 2009, claims 1-6, 8, 9, 11, 12, 15, and 16 stand rejected. Claim 13 is indicated to be allowed if rewritten into an independent form including all the limitations of base claim and intervening claims.

In the instant amendment, claim 1 is amended to more clearly set forth the claimed subject matter. Support for the amendment may be found by, for example the disclosure of the specification, page 27, lines 6-7.

Claim 12 is amended to improve the wordings by changing "region as set forth according to SEQ ID NOs: to read "region of SEQ ID NOs.:."

No new matter is introduced. Entry and consideration of the amendment are respectfully requested.

Response to Rejection Under 35 U.S.C. § 103

In the Office Action, claims 1-6, 8 and 16 are rejected under 35 U.S.C. 103(a) as assertedly being unpatentable over Kitai et al. (Appl. Microbiol. Biotechnol 28(1):52-56 (Mar. 1988); cited in the IDS of 10/9/09) in view of Simmons et al. (Nat. Biotech. 14:629-634 (1996)) and further in view of Sytkowski et al. (WO 99/02709; published 1/21/99); cited in the IDS of 10/9/09).

In the Office Action, claims 1, 9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kitai et al. (Appl. Microbiol. Biotechnol 28(1):52-56 (Mar. 1988); cited in the IDS of 10/9/09) in view of Simmons et al. (Nat. Biotech. 14:629-634 (1996)) and further in view of Sytkowski et al. (WO 99/02709; published 1/21/99); cited in the IDS of 10/9/09) as applied to claim 1 above, and further in view of Lilly (US 20040053370; filed 5/29/03).

In the Office Action, claims 1 and 11 are rejected under 35 U.S.C. 103(a) as being assertedly unpatentable over Kitai et al. (Appl. Microbiol. Biotechnol 28(1):52-56 (Mar. 1988); cited in the IDS of 10/9/09) in view of Simmons et al. (Nat. Biotech. 14:629-634 (1996)) and further in view of Sytkowski et al. (WO 99/02709; published 1/21/99); cited in the IDS of 10/9/09) as applied to claim 1 above, and further in view of Kwon et al. (W0200015661; published 3/23/00).

For the purpose of the prosecution, the Examiner interprets claim 1 as being drawn to a method for producing a Ig Fc in the cytoplasm or *secreted* from an E coli having been transfected with a nucleotide encoding the STII signal sequence and the Ig Fc domain without a variable domain (Claim 1).

Applicants respectfully traverse the rejections.

Kitai is cited as disclosing a penicillinase signal peptide and hIgG-Fc were fused through the one additional amino acid, Ser. Kitai discloses plasmid pEAP8 was an excretion vector in *E.* co/i transformants (Kate e tal. 1987) and containing the DNA region needed for the extracellular production in *E. Coli*, that is KII gene of pMB9, Ex promoter.and penicillinase promoter-signal-peptide. The Examiner states that Kitai does not teach using the heat-stable enterotoxin signal peptide or the constant regions from IgA, IgM, IgE or IgD, or for the subtypes IgG1, IgG2, IgG3 and IgG4.

Simmons and Sytkowski are cited as teaching heat stable enterotoxin (STII) signal sequence derivatives.

On the contrary, currently amended claim 1 clarifies that the immunoglobulin constant region is not secreted into the medium.

The present invention is drawn to a method for mass producing an Fe region using STII as a signal sequence, and an Fc region produced by the method of the present invention is expressed in cytoplasm in a soluble form. The Fc region is not secreted into a medium or the secretion into a medium, if any, is negligible. This method is much more effective than the conventional methods using extracellular secretion vectors which allow target proteins be secreted into the periplasmic space or medium. The degree of secretion into the periplasmic space or medium, aggregation degree after secretion, and expression efficiency of a target protein in a fusion protein form vary greatly from one protein to another protein, depending on the expression vectors, signal sequences, etc. The claimed method makes it possible to produce a target immunoglobulin constant region in an improved efficiency.

Kitai discloses a method for excreting a protein of interest into a medium, as opposed to the present invention that expresses an Fc region to be presented in a cytoplasm without secretion into the medium. Thus, Kitai fails to teach a method to produce a Fc region into a cytoplasm of a host transformant.

With regard to the Examiner's assertion that one skilled in the art would been motivated to replace the penicillinase signal peptide with those taught by Simmons, Applicants respectfully disagree for the following reasons.

Simmons discloses a method for improving protein expression using a STII variant. In an expression vector designing, the selection of a signal peptide with respect to a protein of interest or host cell is one of the most important elements to provide a working vector system.

As such, because Kitai and Simmons have completely different vector systems from each other, a person skilled in the art would not have been motivated to use STII sequence of Simmons to replace the signal sequence of Kitai, without further teachings to do so. Additionally, even if Kitai and Simmons could be combined, the desired protein would be expressed as a secreted protein. A skilled artisan would never have expectation or prediction that that proteins could be expressed in the cytoplasm.

Other cited references, Sytkowski, Lilly and Kown also fail to cure the deficiencies of Kitai and Simmons, discussed above.

Accordingly, Applicants respectfully submit that the rejection is not sustainable and withdrawal is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number **202-775-7588**.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

/Sunhee Lee/

Sunhee Lee
Registration No. 53,892

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Date: February 4, 2010